

In re Application of:
Rheins and Morhenn
Application No.: 09/375,609
Filed: August, 17, 1999
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PATENT
Attorney Docket No.: DERM1100-1

EXHIBIT C:

DECLARATION UNDER 1.132 (DR. GERALD KRUEGER)

PATENT
DERM 1100-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Rheins and Morhenn Art Unit: 1646
Application No.: 09/375,609 Examiner: L. Spector
Filed: August 17, 1999
Title: METHODS AND KITS FOR OBTAINING AND ANALYZING SKIN
SAMPLES FOR THE DETECTION OF NUCLEIC ACIDS (as amended)

Commissioner of Patents
Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. § 1.132

Sir:

I, Gerald Krueger, do hereby declare and state that:

1. I am familiar with the above-identified patent application and the disclosure of methods for obtaining and analyzing skin samples therein.
2. I earned a Doctorate of Medicine degree from Loma Linda University Medical School in Loma Linda, California and I am presently a Professor and Cumming Presidential Endowed Chair in the Department of Dermatology at The University of Utah Health Science Center.
3. I have conducted research in the area of dermatological disorders, genetic engineering of skin cells along with research that assesses drugs into and out of skin in health and disease for over thirty years, and have published numerous papers regarding these topics.
4. I understand that claims 64, 65, 76, 85, 86, and 161-162 stand rejected under 35 U.S.C. § 102 as anticipated by Garofano et al., *Adv. Forensic Haemogenet.*, 6:281-83 (1996), and that claim 70 stands rejected as anticipated by, or in the alternative under 35 U.S.C. § 103, as obvious over Garofano et al.
5. I understand that claims 71-72 and 80-82 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Garofano et al.

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6. I understand that claims 77-78, 80-83, 149-154, 156-158, and 163 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Garofano et al. in view of Paludan et al., *J. Invest. Derm.* 99:830-35 (1992).

7. I understand that claim 155 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Garofano et al. in view of Paludan et al., and further in view of Ramsay et al., U.S. Pat. No. 6,056,859 and Furcht et al., U.S. Pat. No. 6,054,277.

8. I understand that claim 87 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Garofano et al. in view of Frayne, U.S. Pat. No. 5,811,239.

9. I have reviewed Garafano et al., Paludan et al., Ramsay et al., Furcht et al., and Frayne.

10. Based on the teachings of these cited references, a dermatologist or a scientist working in the area of dermatological disorders and/or dermatological nucleic acid sampling methods, would not have concluded that there was a reasonable chance of success that the method used by Garafano et al. allegedly to isolate DNA from the epidermis, could be successfully employed to isolate RNA, based on known difficulties in obtaining useful RNA samples compared to DNA samples, and the known fact that the skin is a rich source of RNAases.

11. Based on the teachings of these cited references, a dermatologist or a scientist working in the area of dermatological disorders and/or dermatological nucleic acid sampling methods, would not have concluded that there was a reasonable chance of success that the method used by Garafano et al. allegedly to isolate DNA from the epidermis, could be successfully employed to isolate detectable quantities of RNA, because Paludan et al. report that "the RNA yield was too small for measurement," and appeared to be below 50 pg, even though they sampled the skin by scraping it until the scraped area was moist, which would be expected to provide a larger skin sample than the tape stripping method employed by Garafano et al.

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(Paludan et al., pg. 831, last paragraph, right column, pg., 832 third full paragraph, left column, and figure 4).

12. Based on the teachings of these cited references, a dermatologist or a scientist working in the area of dermatological disorders and/or dermatological nucleic acid sampling methods, would not have concluded that there was a reasonable chance of success that the method used by Garafano et al. allegedly to isolate DNA from the epidermis, could be successfully employed to isolate detectable quantities of RNA, because despite the fact that Garafano et al. analyzed DNA, which would be expected to be easier to isolate and more abundant in a sample than RNA, they conclude that they obtained a "low percentage of positive results" and suggest that this was the result of the extremely small amount of nucleic acids in the sample (See Garafano et al., pg. 282, last 2 paragraphs).

13. The fact that a dermatologist or a scientist working in the area of dermatological disorders and/or dermatological nucleic acid sampling methods, would not have concluded that there was a reasonable chance of success that the method used by Garafano et al. allegedly to isolate DNA from the epidermis, could be successfully employed to isolate RNA, is further established by the lack of any published report of which I am aware, in the over six years since the publication of Garafano et al. and over ten years since the publication of Paludan et al., of the use of tape stripping to obtain RNA samples from skin, other than the work of the present inventors or their assignee, DermTech International.

14. Based on the teachings of the cited references, a dermatologist or a scientist working in the area of dermatological disorders and/or dermatological nucleic acid sampling methods, would not have considered the results of Garafano et al. conclusive with respect to successfully isolating DNA from the epidermis, because control data is not presented by Garafano et al. to confirm that the DNA was not a contaminant in the nucleic acid amplification methods used.

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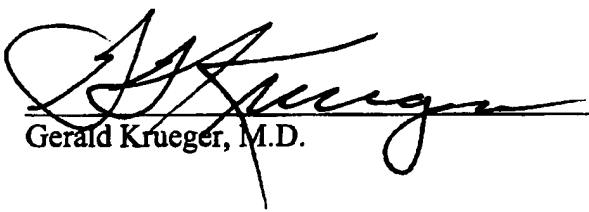
15. When I first learned of the present invention, despite being knowledgeable about state-of-the-art dermatological sampling methods, including adhesive tape stripping methods used for drug studies, I was surprised that adhesive tape stripping could be used to obtain RNA samples from the skin because the skin is an abundant source of nucleases, including RNAases.

16. I was not surprised, however, to learn that the more invasive approach, scraping the skin to near bleeding, of Paludan et al., could be used to isolate mRNA, as this method harvests viable cells in large numbers, which are expected to provide sufficient mRNA to allow isolation and detection of RNA despite the presence of RNAases in the skin.

17. I further declare that all statements made herein of knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine, or imprisonment, or both under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date

9/8/03


Gerald Krueger, M.D.